

## CLAIMS

1. A composition for expression of a DNA coding sequence in a recipient, the composition comprising a polymer microparticle and DNA, wherein the DNA is in aqueous solution, is inside the microparticle and comprises said coding sequence, and wherein the microparticle is 10 $\mu$ m or less in diameter and induces expression of said coding sequence following oral administration to a recipient.
2. A composition according to Claim 1, wherein the polymer is soluble in organic solvent and thereby suitable for formation of microparticles by solvent extraction.
3. A composition according to Claim 1 wherein the DNA is plasmid DNA.
4. A composition according to Claim 1 wherein the DNA comprises a sequence promoting transcription of the coding sequence.
5. A composition according to Claim 1 is non-toxic and pharmaceutically acceptable and wherein the microparticle consists of or comprises a bio-degradable polymer.
6. A composition according to Claim 5 wherein the polymer is selected from the group consisting of a lactide containing polymer, a glycolide-containing polymer, and a polymer comprising lactide and glycolide.
7. A composition according to Claim 1 wherein the microparticle is greater than 0.1  $\mu$ m in diameter.
8. A composition according to Claim 1 wherein the DNA codes for an immunogen.

9. A composition according to Claim 8 wherein the DNA codes for a immunogenic component of a pathogenic organism selected from the group consisting of pathogenic bacteria and pathogenic viruses.

10. A pharmaceutical composition comprising a plurality of polymer microparticles and a pharmaceutically acceptable carrier, wherein the microparticles contain an aqueous solution of DNA that comprises a sequence coding for a polypeptide, wherein the microparticle is adapted to induce expression of the polypeptide following administration to a recipient, and wherein the polypeptide is selected from:-

- (a) the antigens FHA, PT, 68kd-Pertactin, tetanus toxin, gp48, NS1, Capsid, gp350, NS3, SA, I, NP E, M, gp340, F, H, HN, 35kd protein, BP1, E1, E2, C, M, E and MSHA according to table 1; and
- (b) immunogenic fragments, variants and derivatives of the polypeptides of (a).

11. A composition according to Claim 10 comprising microparticles of 10  $\mu\text{m}$  or less in diameter.

12. A composition according to Claim 11 comprising double-stranded DNA selected from (i) plasmid DNA and (ii) DNA derived from plasmid DNA by one or more of insertion, deletion and substitution.

13. A composition according to Claim 12 wherein the DNA comprises a sequence promoting transcription of the coding sequence.

14. A composition according to Claim 10 wherein the microparticle is non-toxic and pharmaceutically acceptable and consists of or comprises a bio-degradable polymer.

15. A composition according to Claim 14 wherein the polymer is a lactide

containing polymer.

16. A composition according to Claim 14 wherein the polymer is a glycolide-containing polymer.

17. A composition according to Claim 14 wherein the polymer comprises poly (DL-lactide-co-glycolide).

18. A composition according to Claim 10 wherein at least 50% of the microparticles are in the size range 0.1  $\mu\text{m}$  to 10  $\mu\text{m}$ .

19. A vaccine for eliciting antibodies against an immunogen, comprising a composition according to Claim 10 and a pharmaceutically acceptable carrier, wherein the DNA sequence codes for said immunogen.

20. A vaccine according to Claim 19 further comprising a taste-enhancing agent.

21. A vaccine according to Claim 19, comprising first and second vaccine components, the first vaccine component comprising DNA inside a microparticle wherein the DNA includes a sequence coding for an immunogen and wherein the microparticle has a first half-life *in vivo*, and a second vaccine component comprising DNA inside a microparticle, wherein the DNA contains a sequence coding for an immunogen and wherein the microparticle has a second half-life *in vivo*.

22. A vaccine according to Claim 21 wherein the immunogen of the first vaccine component and the immunogen of the second vaccine component are the same.

23. A vaccine according to Claim 21 wherein the first and second half-lives are, respectively, up to 2 weeks and more than 2 weeks.

0989105-070301

24. A composition comprising polymer-encapsulated DNA and having a water content of less than 5%, obtained by freeze-drying a composition according to Claim 1.

25. A method of encapsulating an aqueous solution of DNA in a polymer microparticle, comprising

- providing a (water-in-oil)-in-water emulsion containing the DNA solution; and

- adding this emulsion to excess of a further aqueous phase to extract the oil phase and thereby form microparticles,

wherein the further aqueous phase is at elevated temperature.

26. A method according to Claim 25 wherein extraction of the oil phase is carried out using a further aqueous phase at a temperature of 25°C or above.

27. A method according to Claim 26 wherein extraction of the oil phase is carried out using a further aqueous phase at a temperature of 30°C or above.

28. A method according to Claim 25 comprising preparing an aqueous solution of DNA and alcohol with an alcohol content of 1 to 40%.

29. A method according to Claim 25 comprising forming microparticles in the size range 0.01  $\mu\text{m}$  to 30  $\mu\text{m}$ .

30. A method according to Claim 25 wherein the DNA is circular, plasmid DNA, or circular plasmid-derived DNA.

31. A method according to Claim 25 wherein the further aqueous phase is at

least 5°C higher in temperature than the (water-in-oil)-in-water emulsion.

00393175-07004  
F00040-00000000